

"Never settle for anything less than what you deserve. It's not pride, it's self-respect"

CSIR NET – Life Science

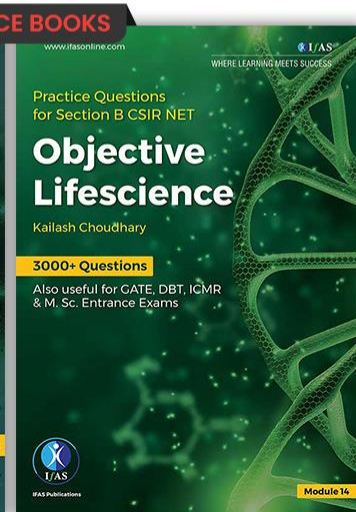
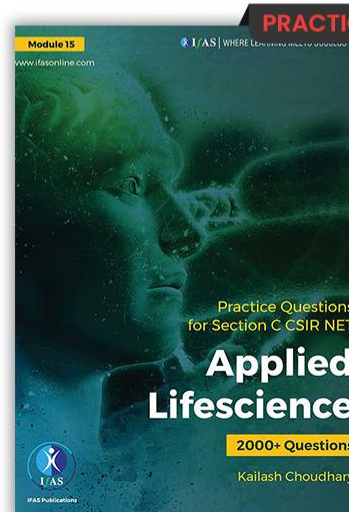
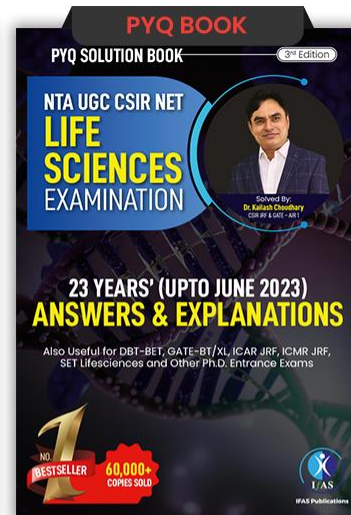
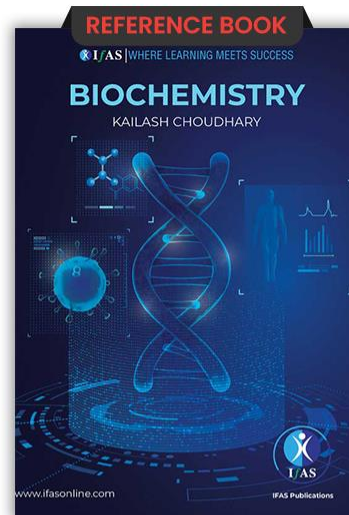
Unit 1: Biochemistry

16

Nucleotide and Vitamin Metabolism



Order Online and Get
Free Delivery Across India





Points to be covered in this Lecture



Pyrimidine Biosynthesis



Pyrimidine Catabolism



Vitamin A, D, E and K

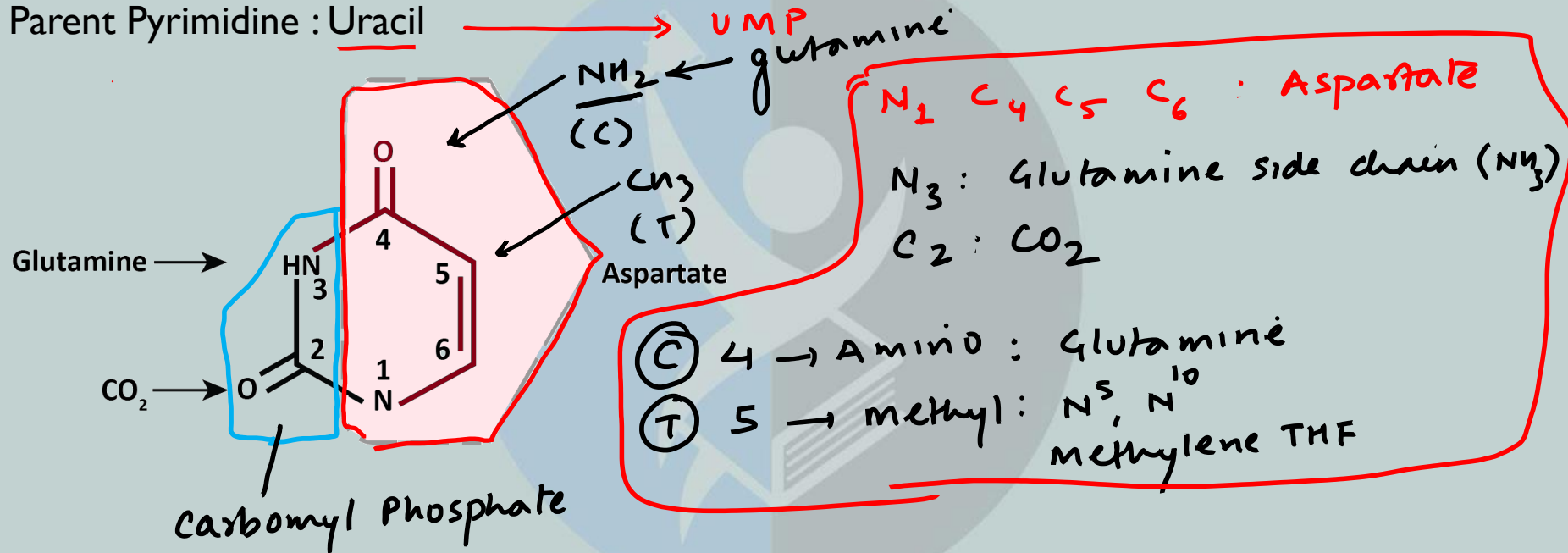


Vitamin B complex



Vitamin C

SYNTHESIS OF PYRIMIDINE RIBONUCLEOTIDES

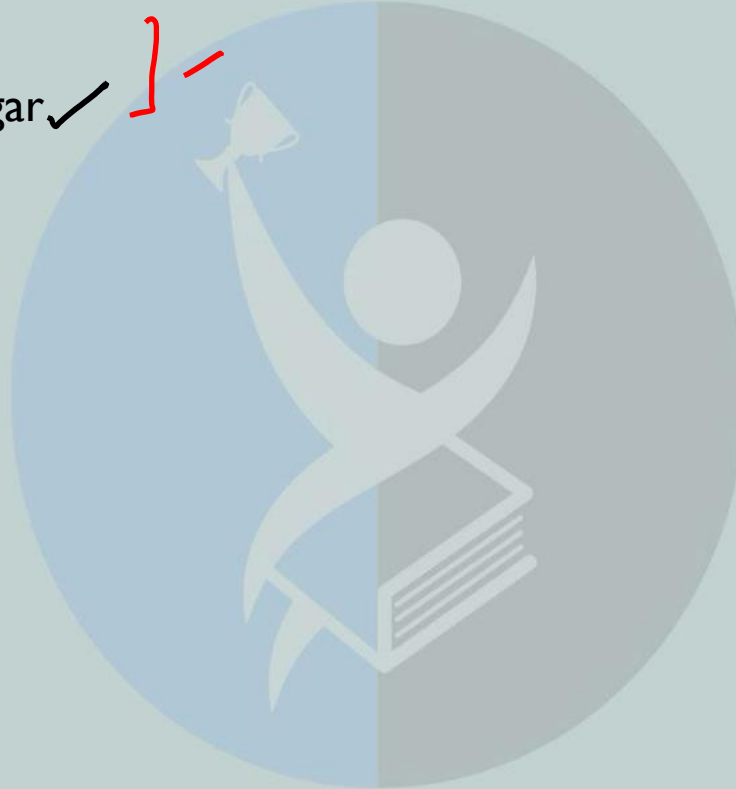
Pyrimidine De novo biosynthesisParent Pyrimidine : Uracil

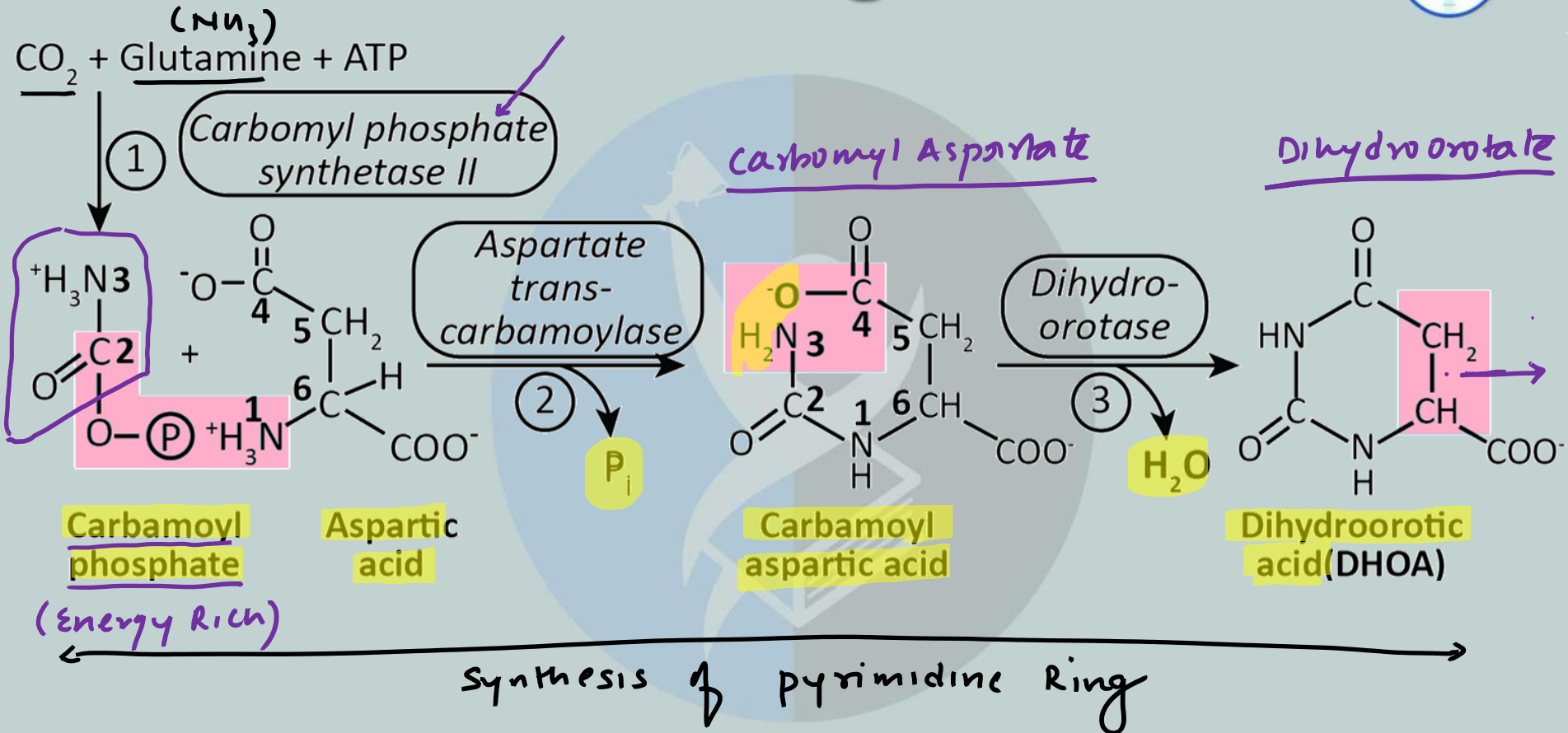


Series of Events:

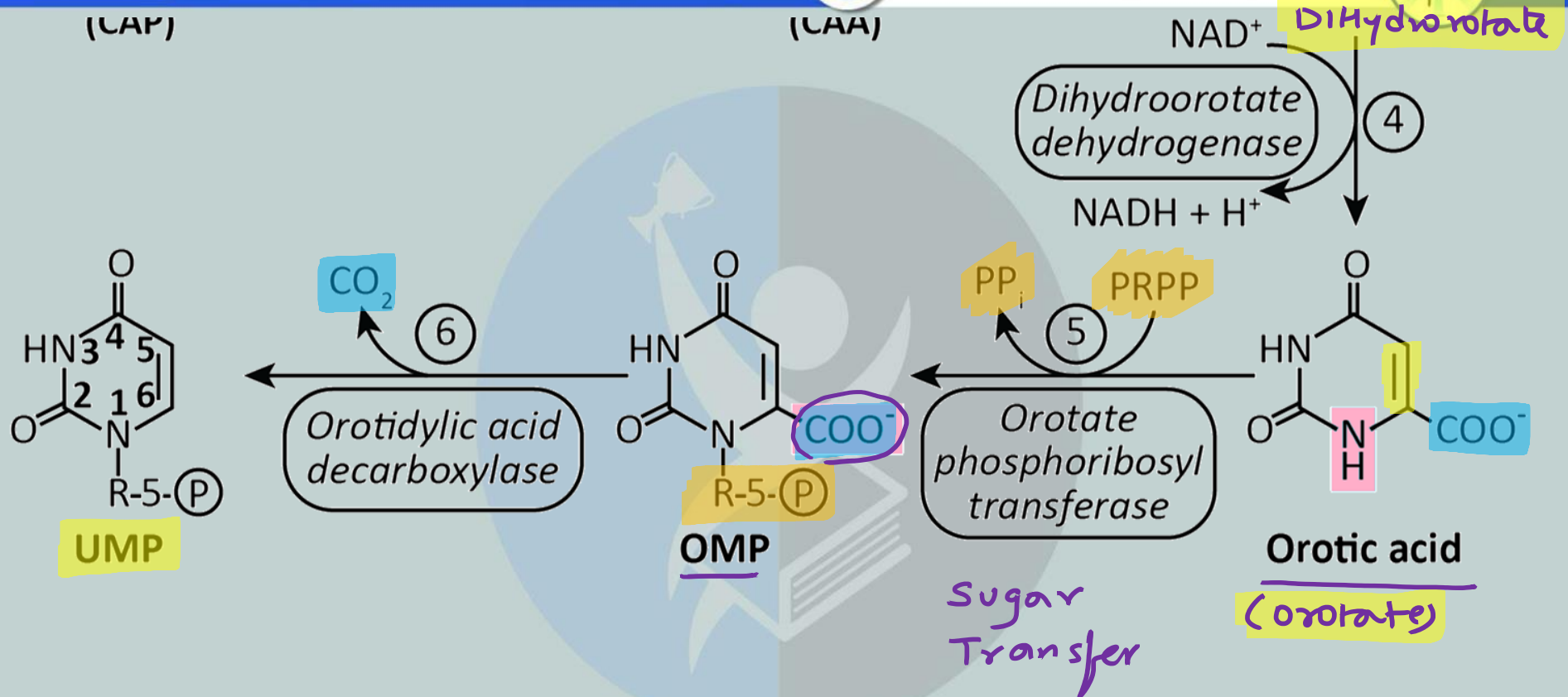
1. Pyrimidine Ring ✓

2. Transfer to Pentose Sugar ✓





(CAP)





Regulatory Step



✓
Aspartate
Transcarbamylase
(ATCase)

← ⊕ AMP, GMP
| ⊖ UMP, CMP

Carbonyl - Aspartate + P

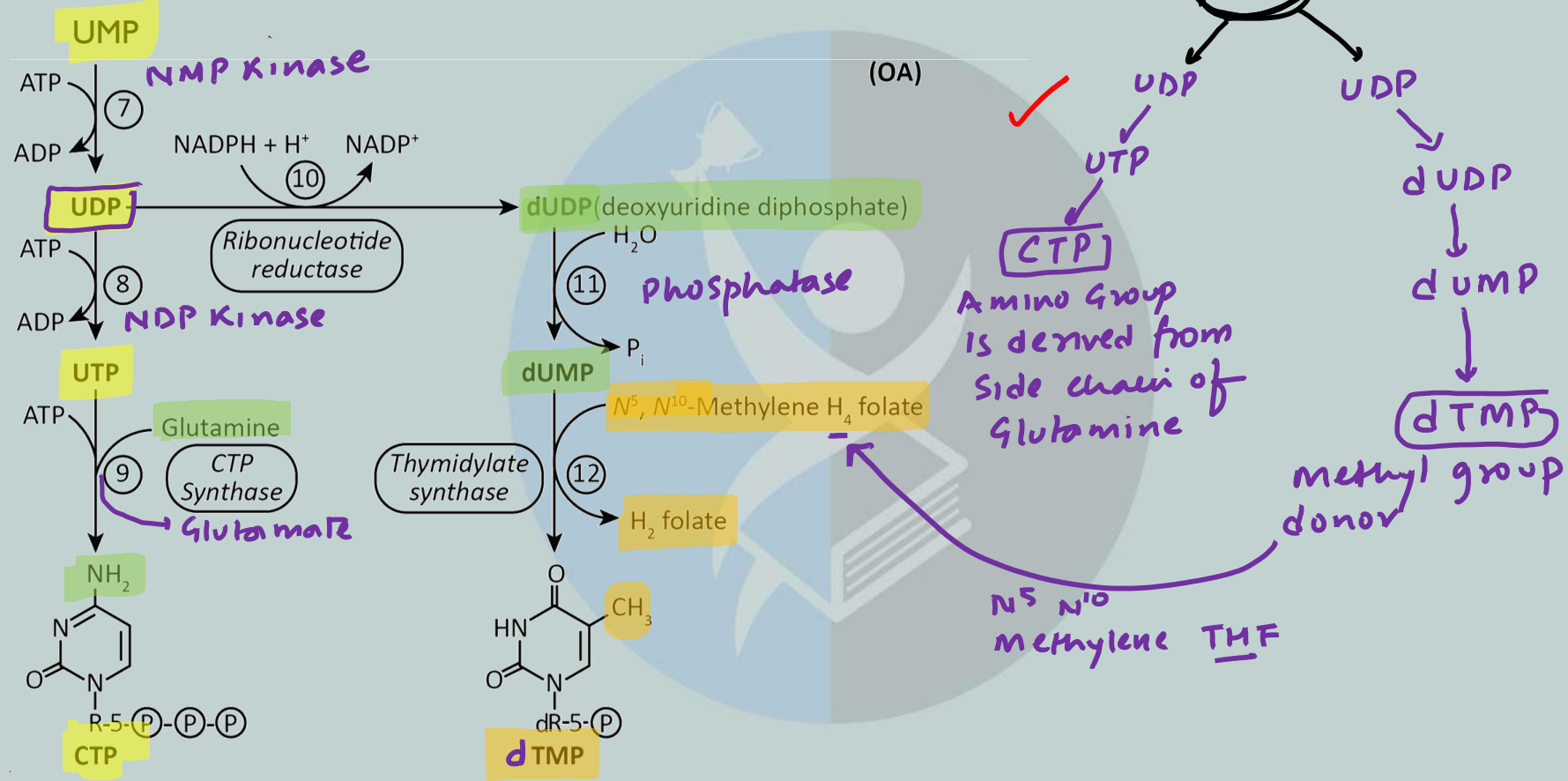
Dihydroorotate

Orotate

OMP

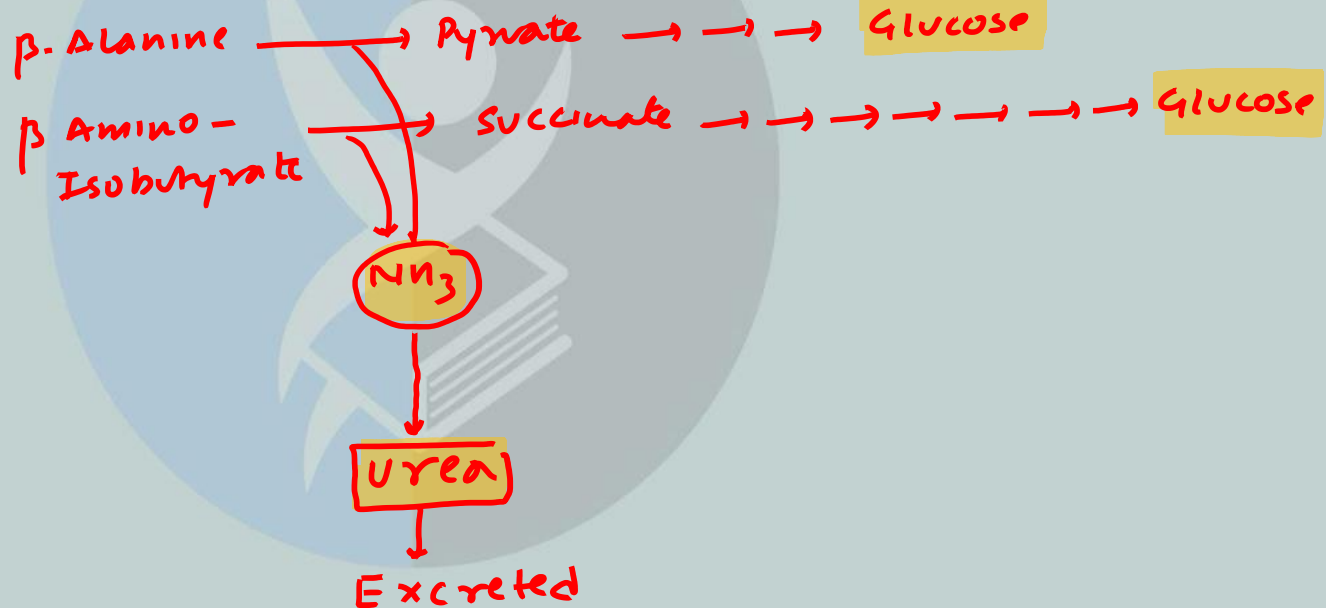
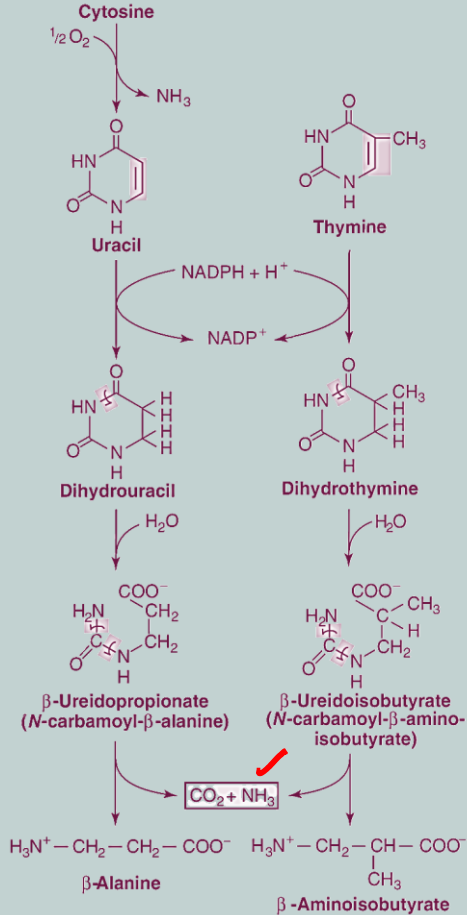
UMP

Cytosine and Thymine nucleotide biosynthesis



Degradation of pyrimidine nucleotides

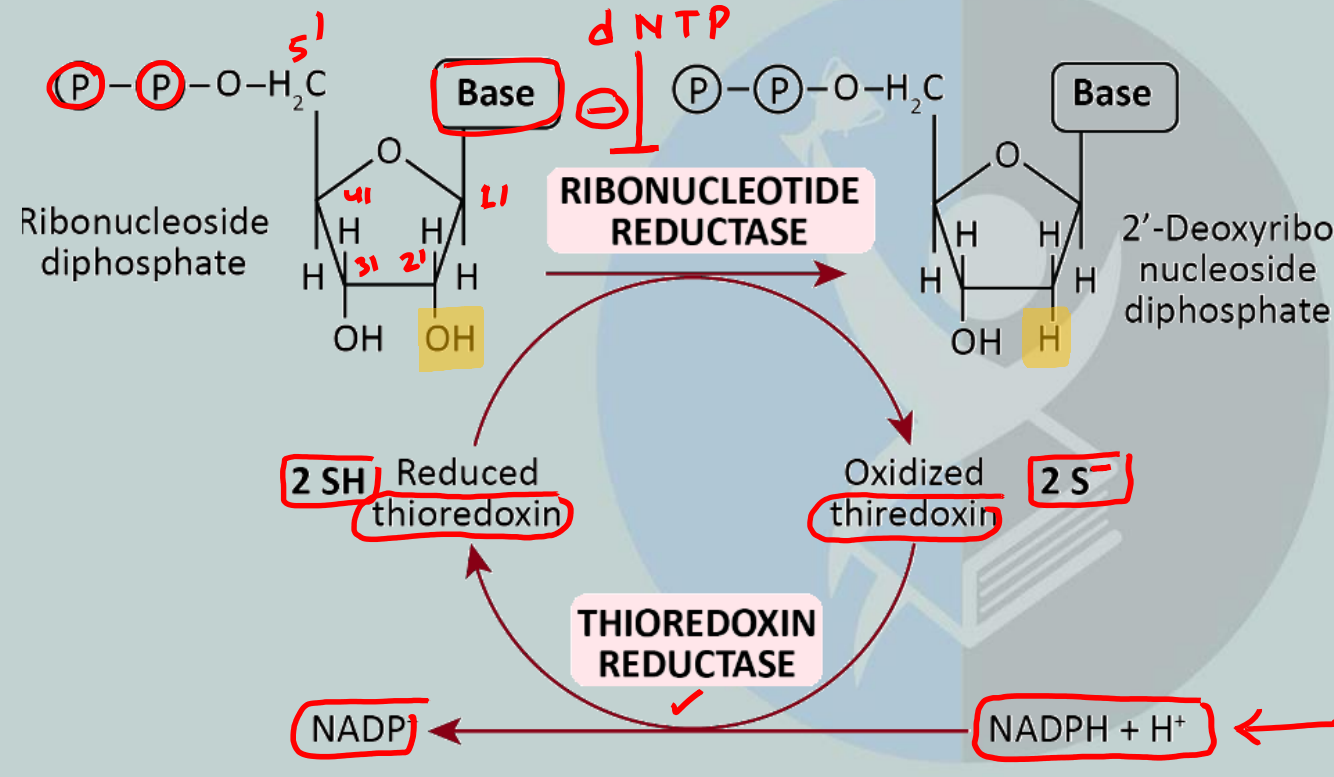
- Glucogenic
- Waste N is eliminated in form urea.



Conversion of ribonucleotides to Deoxyribonucleotides : ~~Ribonucleotide reductase~~

- It act on NDP

NDP \longrightarrow dNDP





Vitamins

- Essential nutrient
- Req^d in small amount
- Role in growth, dev^{op} & metabolism

Fat Soluble (ADEK)

- Absorbed along with dietary fat
- Can be stored in the body's fatty tissues and liver
- Toxic in high doses



Water Soluble (BC)

- Absorbed directly into the bloodstream
- Not stored in large amounts in the body
- Excess amounts are typically excreted.





I. VITAMIN A: RETINOID AND CAROTENOIDS

1. A primary alcohol containing a β -ionone ring with an unsaturated side chain

2. Occurs in three forms:

- **Retinol:** Esters of retinols stored in liver
- **Retinal:** Isomerization plays role in vision
- **Retinoic acid:** Cell differentiations

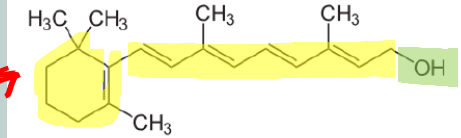
Precursor: β -carotene

[Golden Rice]

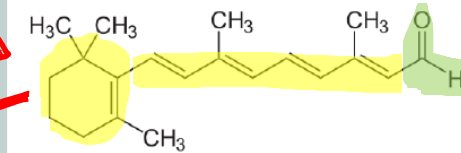
Dietary source: Liver, carrots, and dairy.

Retinol
Dehydro-
genase

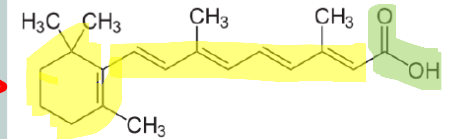
Retinal
oxidase
(irreversible)



Retinol



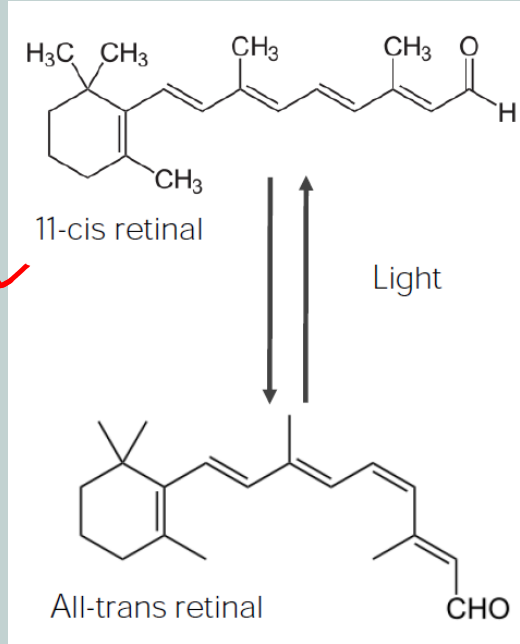
Retinal



Retinoic acid



I. Role of Retinal in Vision



light

11-cis Retinal + **opsin** = **Rhodo-opsin**

Dark
↓
All trans Retinal

Protein is a
GPCR
⊕

βγ + **Gαt** (Transducin)

⊕
Phosphodiesterase

↓ **C-GMP** → GMP

- Na^+ channel close
- Rod cell membrane hyperpolarization
- Signal to visual cortex of brain through optic neurons.



2. Role of retinoic acid

- Irreversibly made from **retinal**
- **Morphogen:** Anterior/posterior development through **hox genes**.
- **Strongly teratogenic** (*developmental defect*)
- Acts through retinoic acid receptor (RAR)/retinoid x-receptor (RXR) to activate transcription of RARE genes.
- RAR binds to a DNA sequence known as the Retinoic Acid Response Element (RARE)

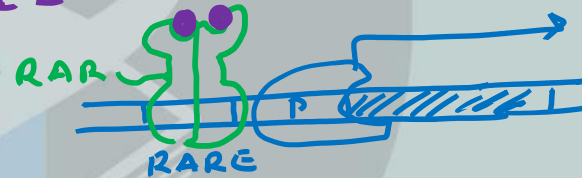
→ *Limb formation*
 fore limb : Tbx 5
 Hind limb : Tbx 4

↳ *Nuclear Receptor family Type II*

Growth:

Low amount of RA

- Keratinization of taste buds
- Slow growth of bones





4. Reproduction

- Supports spermatogenesis in the male
- Preventing fetal resorption in the female
- Retinoic acid alone if given: birth are blind and sterile

5. Maintenance of epithelial cells:

Essential for normal differentiation of epithelial tissues and mucus secretion

6. Role in immunity and cancer

- Role in differentiation of immune system cells

↳ of RBC
↳ No division



Deficiency disorder

- Night blindness
- Prolonged deficiency leads to xerophthalmia:

Keratinization of the cornea and skin and blindness.

High vitamin A (Isotretinoin) is teratogenic

↘ creams
(Acne)



VITAMIN D

Ergocalciferol (vitamin D₂): Plants

Cholecalciferol (vitamin D₃): Animals

The active form: 1,25-dihydroxycholecalciferol (1,25 diOH D₃), ← Calcitriol

It binds to intracellular receptor proteins. ← Nuclear Family Receptor Type II

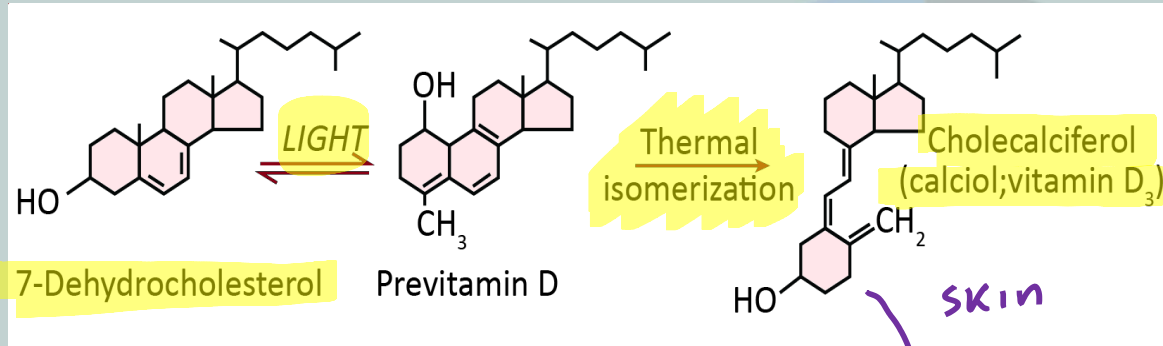
Regulation of calcium absorption and homeostasis

Intake : Sun exposure, fortified foods, fish oils, Dairy products

UV - A



Vitamin D is synthesized in the **skin** by exposure of **sunlight (UV-A)**





Metabolism of vitamin D to Calcitriol

Calcidiol (Active) → Calcidiol → Calcidiol

Liver

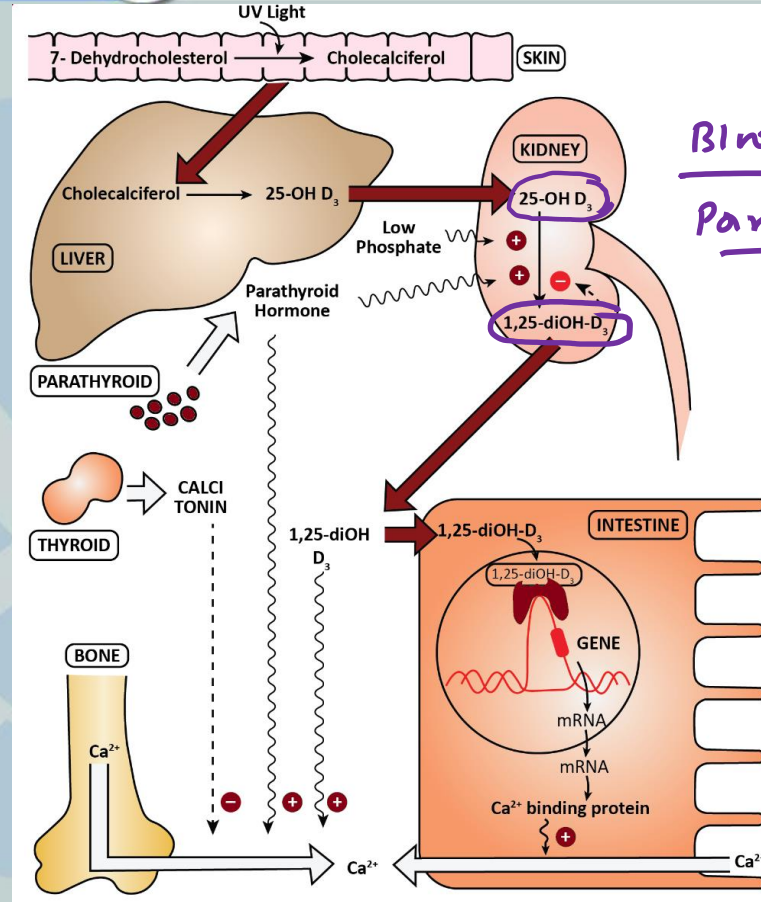
Cholecalciferol is hydroxylated to form the 25-hydroxy derivative calcidiol (25-OH D₃)

Released into the circulation bound to a vitamin D-binding globulin

Kidney

Calcidiol hydroxylation to yield the active metabolite 1,25-dihydroxy vitamin D (calcitriol)

Active → Gene level



Blood Ca²⁺ ↓
Parathormone ↑



Function of vitamin D (calcitriol \rightarrow 1,25 Dihydroxy chole calciferol D_3)

- Increasing uptake of calcium by the intestine,
- Minimizing loss of calcium by the kidney, and
- Stimulating resorption of bone when necessary.



Vitamin D deficiency

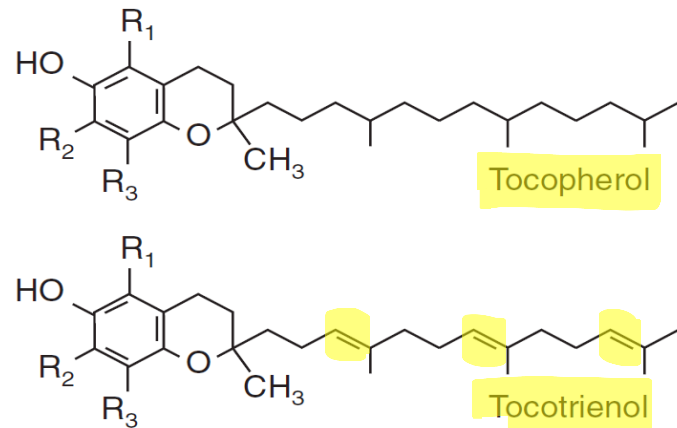
Rickets: the bones of children are undermineralized as a result of poor absorption of calcium.

Osteomalacia: in adults results from demineralization of bone in person who have little exposure to sunlight,



VITAMIN E

- Fat-soluble vitamin
- Consists of numerous compounds **Tocopherols** and the **tocotrienols**
- Act like **antioxidants**
- **Inhibits** production of **reactive oxygen species** (O_2^- , H_2O_2)
- Most **abundant** in **wheat germ**, **sunflower**, and **safflower oils**
- Acts **counter** to **vitamin K** and may be danger to **clotting** in excess

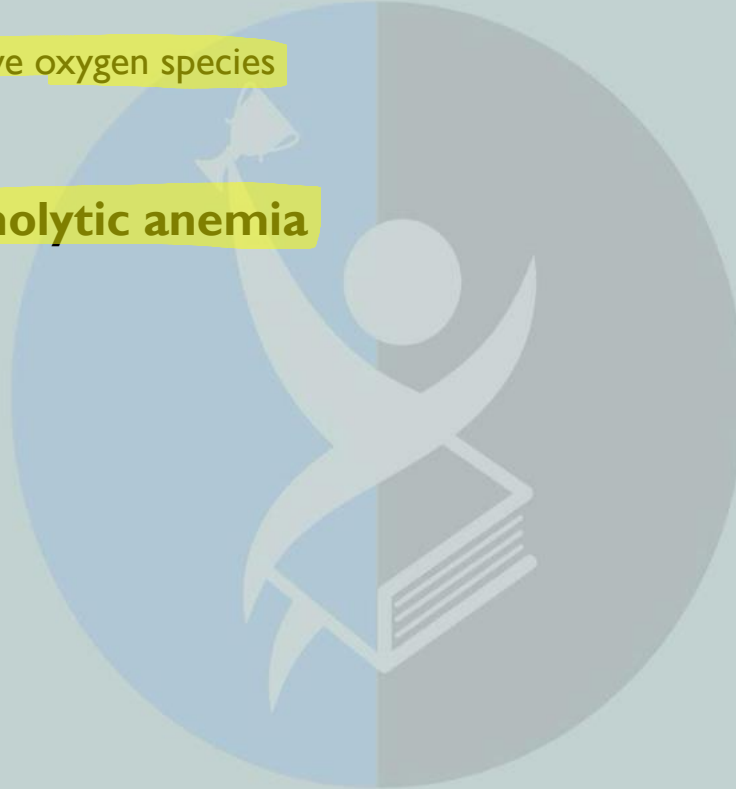




Antioxidant Functions

- Prevents damage from reactive oxygen species
- Protects membrane lipids

Dietary Deficiency: hemolytic anemia



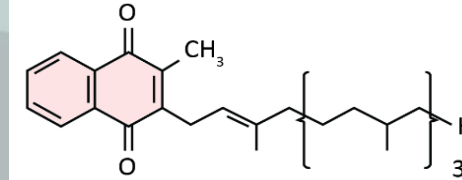


VITAMIN K

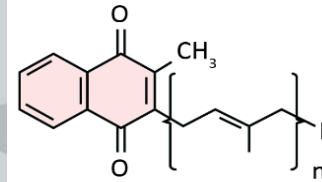
Phylloquinone: Green vegetables

Menaquinones: Synthesized by **intestinal bacteria**

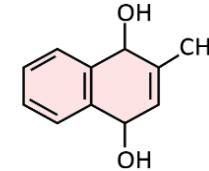
Fat-soluble vitamin with roles in **blood clotting** and **bone health**



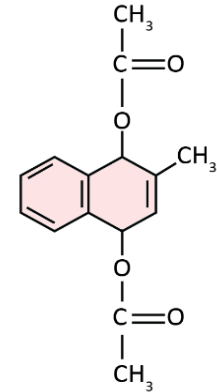
Phylloquinone



Menaquinone



Menadiol



Menadiolo diacetate
(acetomenaphthone)

Poly terpenes



Carboxylation of Glutamate of blood clotting factors II, VII, IX, X : γ -carboxylase

warfarin
↓
⊖

Vitamin K epoxide → Vitamin K quinone → Vitamin K hydroquinone

Vitamin K hydroquinone which is used for Gamma carboxylation

vit K act
as co-enzyme

vit K
epoxide



Deficiency of vitamin K:

Hypoprothrombinemia

↳ slow blood clotting





THIAMINE (VITAMIN B1)

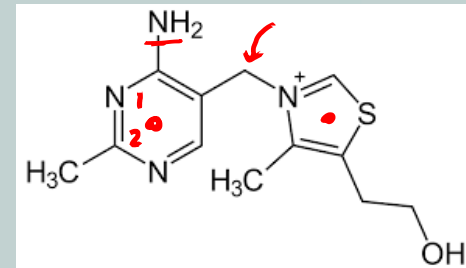
Pyrimidine and a thiazole ring linked by a methylene bridge.

Source : Whole grains, meat (especially pork), nuts, beans, and seeds.

Role in carbohydrate metabolism – Aldehyde group transfer

Co-enzyme - Thiamine pyrophosphate (TPP)

1. Pyruvate dehydrogenase ← Linkage step
2. Pyruvate decarboxylase ← Alcoholic fermentation
3. α - Keto Glutarate dehydrogenase ← TCA
4. Transketolase ← PPP





Deficiency disorders:

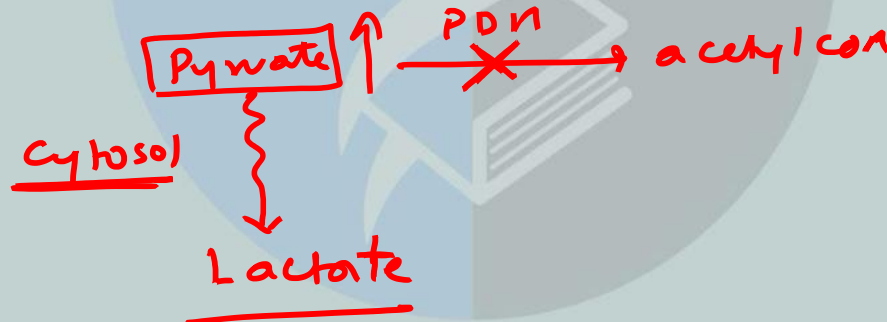
1. Beriberi

Heart = ↑

Infantile beriberi include tachycardia, vomiting, convulsions, and, if not treated, death.
Adult beriberi is characterized by dry skin, irritability, disorderly thinking, and progressive paralysis.

2. Wernicke-Korsakoff Syndrome: Alcoholism

3. Lactate acidosis





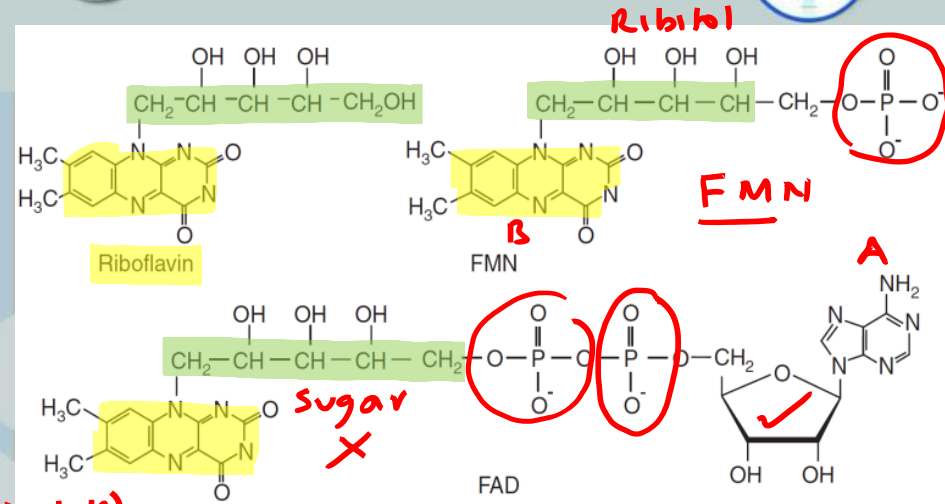
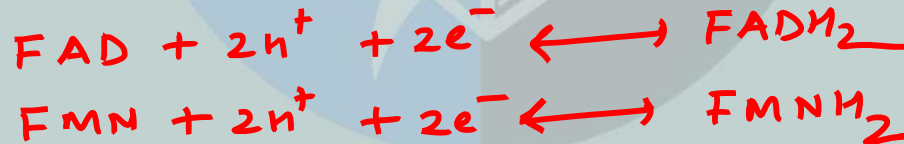
RIBOFLAVIN (VITAMIN B2)

Flavin moiety (isoalloxazine ring) linked to a ribitol side chain

Role in metabolism as the coenzymes

- Flavin mononucleotide (FMN) (Not nucleotide)
- Flavin adenine dinucleotide (FAD) : 1 nucleotide

✓ Electron carriers in oxido-reduction reactions





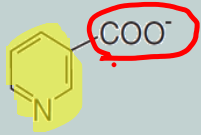
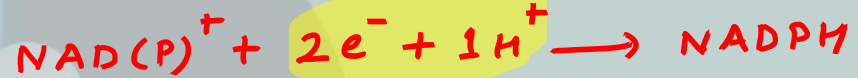
Riboflavin Deficiency

Ariboflavinosis

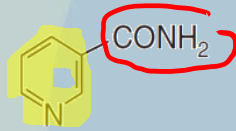
- ✓ Dermatitis
- ✓ Cheilosis (fissuring at the corners of the mouth)
- ✓ Glossitis (the tongue appearing smooth and purplish).

NIACIN (VITAMIN B3)

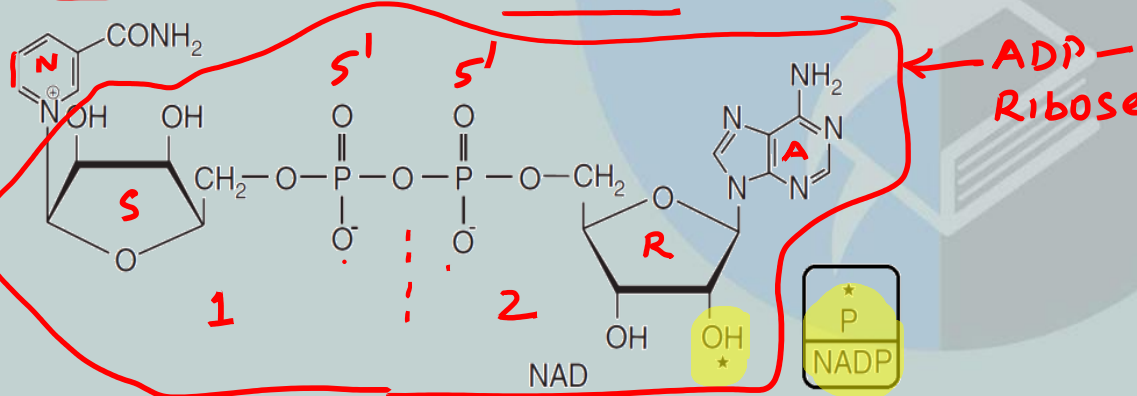
- Niacin, or nicotinic acid, is a substituted pyridine derivative
- Precursor: Tryptophan ✓
- **NAD⁺** and **NADP⁺** serve as coenzymes in oxidation-reduction by accepting a hydride ion
- **NAD** is the source of **ADP-ribose**



Nicotinic acid



Nicotinamide





Treatment of hyperlipidemia

→ Decrease LDL in blood

B_3

Deficiency Disorder

Pellagra: Dermatitis, diarrhea, dementia (3 D)



PENTOTHENIC ACID (VITAMIN B5)

Consists of a β -alanine and a pantoic acid, linked together by a peptide bond.

- Coenzyme A
- Acyl Carrier Protein

- Acyl Chain transfer
- Deficiency rare

} Lipid metabolism



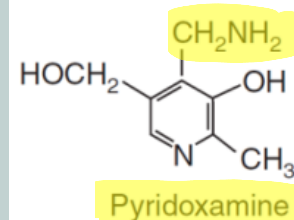
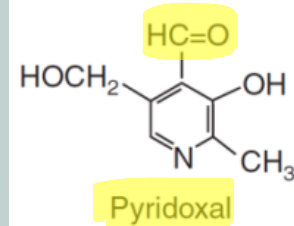
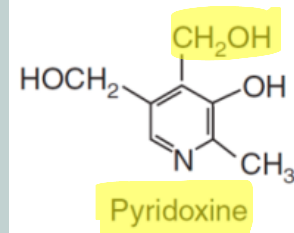
PYRIDOXINE (VITAMIN B6)

Exists in several forms, including pyridoxine, pyridoxal, and pyridoxamine.

Pyridoxal phosphate (PLP) and pyridoxamine phosphate (PMP) are the active coenzyme forms.

Amino acid metabolism, including transamination, deamination, and decarboxylation.

Synthesis of neurotransmitters such as serotonin, dopamine, and gamma-aminobutyric acid (GABA),





Roles in Amino acid Metabolism

Reaction type	Example
Transamination	Oxaloacetate + Glutamate \rightleftharpoons Aspartate + α -Ketoglutarate
Deamination	Serine \rightarrow Pyruvate + NH_3
Decarboxylation	Histidine \rightarrow Histamine + CO_2
Condensation	Glycine + Succinyl CoA \rightarrow δ -Aminolevulinic acid

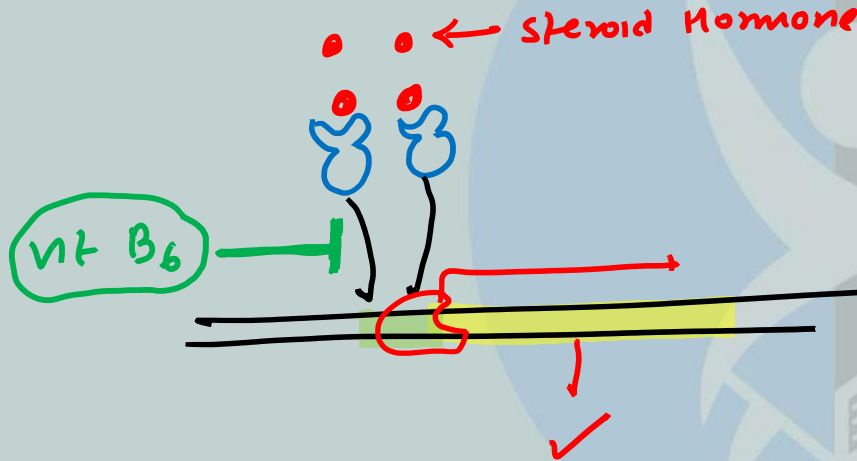
PLP
↓
Amino group transfer

↓
↓
↓
Porphyrin IX
↓ Fe^{2+}
Heme
↓
Hemo-globin
globin



Vitamin B₆ is important in steroid hormone action where it removes the hormone-receptor complex from DNA binding, terminating the action of the hormones.

In vitamin B₆ deficiency, this results in increased sensitivity to the actions of low concentrations of estrogens, androgens, cortisol, and vitamin D.





Deficiency disorder

Heme biosynthesis during erythropoiesis is affected.

Leads to **sideroblastic anemia**

Isoniazid (isonicotinic acid hydrazide), can induce a B6 deficiency by forming an inactive derivative with pyridoxal phosphate

→ Treatment of Tuberculosis



BIOTIN (Vitamin B7/Vitamin H)

Consists of a ureido ring fused with a tetrahydrothiophene ring.

Biotin acts as a coenzyme for carboxylase enzymes.

- Acetyl-CoA Carboxylase → FA biosynthesis
- Pyruvate Carboxylase → Gluconeogenesis
- Propionyl-CoA Carboxylase → odd carbon FA metabolism

Deficiency disorder : Rare

→ Biotin has high affinity for avidin protein

- Lowest K_d value.

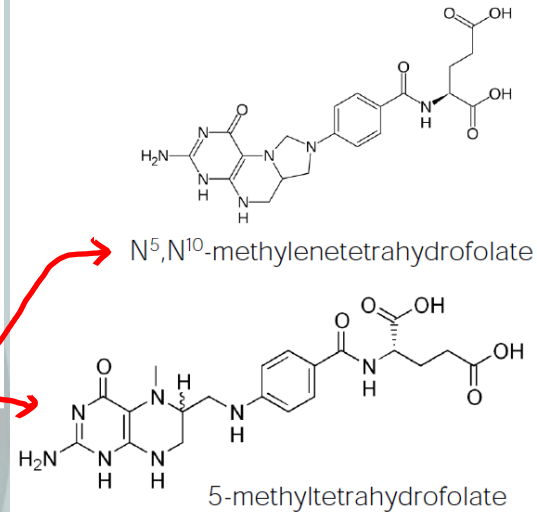
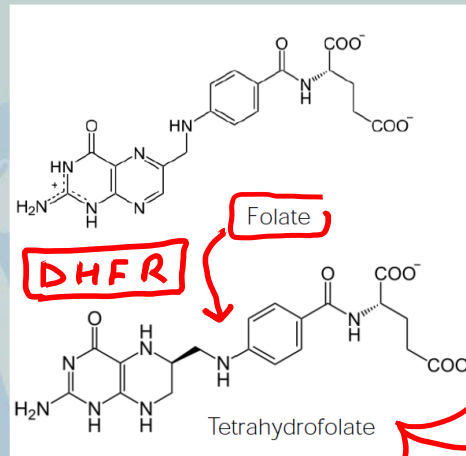
FOLIC ACID (B9)

Folic acid plays an important role in **one-carbon metabolism**,

→ Formyl or methyl group donor (1C)

Folates are important in many metabolic processes:

- Purine synthesis; } N^5 -formyl THF
- Thymidine synthesis; } N^5, N^{10} -methylene THF
- Methionine synthesis; } N^5 -methyl THF
- Serine/glycine metabolism



N^5 -formyl THF



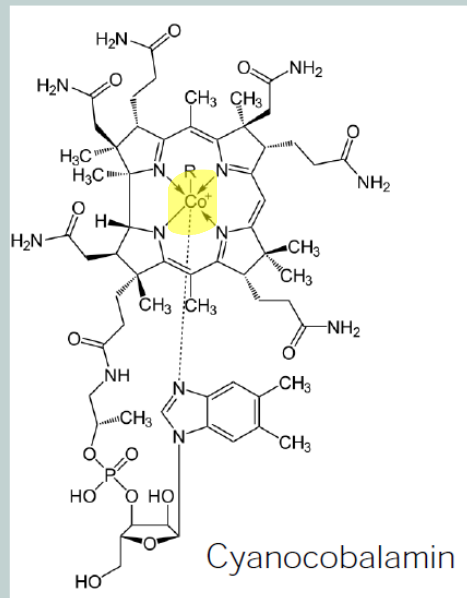
Folate deficiency:

- **Megaloblastic anemia**
- **Spina bifida** and **anencephaly**, the most common neural tube defects

↳ developing child
↳ mother take low amount of folate.

COBALAMIN (VITAMIN B₁₂)

- **Not made in plants**
- Obtained in diet from **meat** and **dairy products**
- Cobalamin contains a **corrin ring** with **cobalt metal**



Bioactive forms

- **Methylcobalamin** (cytosol)
- **Adenosylcobalamin** (mitochondria)

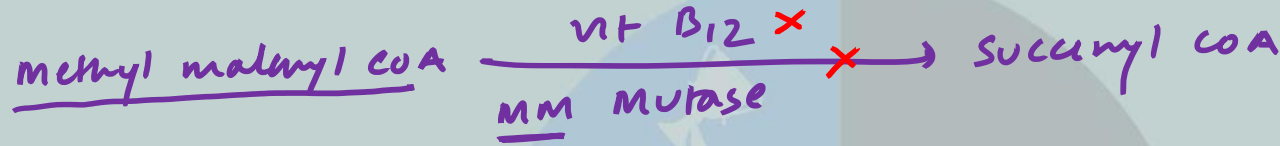
- Needed for metabolism of methionine, propionic acid and neurotransmitters

Synthetic form
↓
Cyanocobalamin

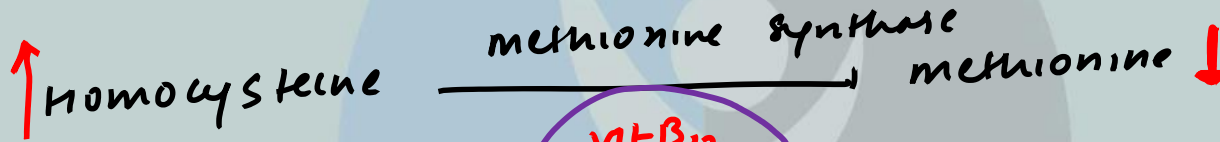
Co-enzyme
✓



Act as Co-enzyme



Peripheral
Neuropathy



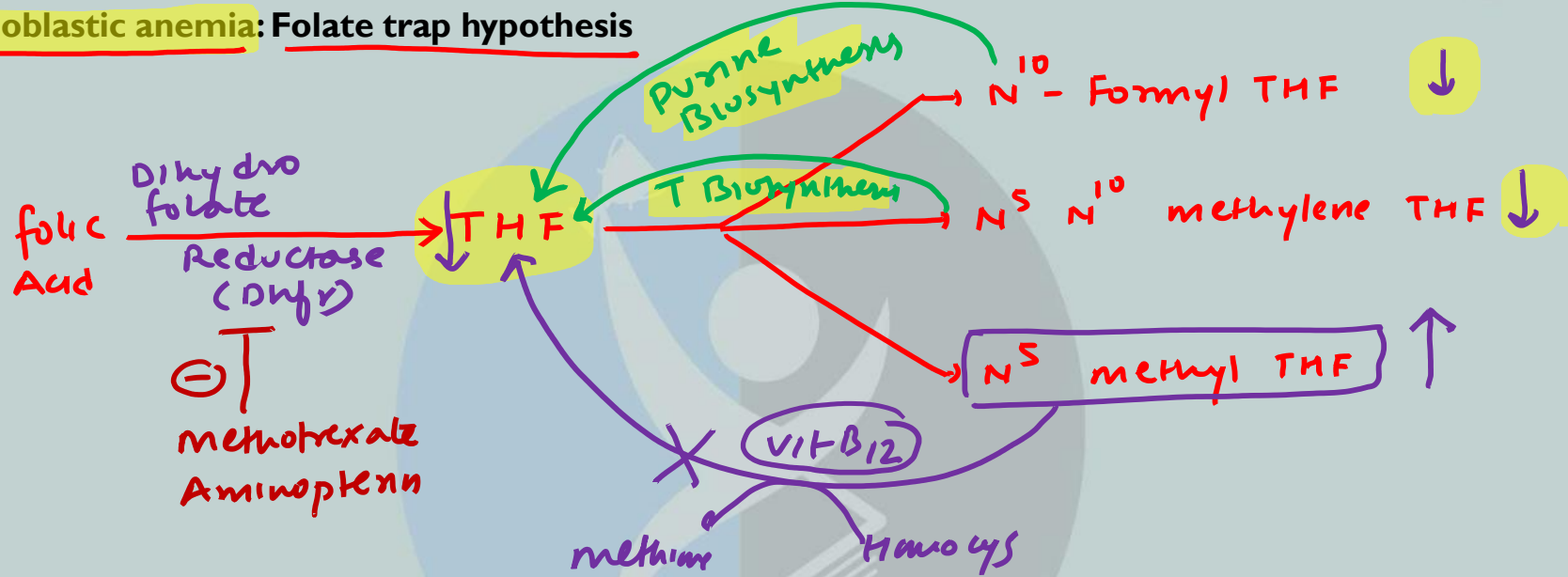
\uparrow N⁵-methyl
THF

vit B_{12}
X

THF ↓

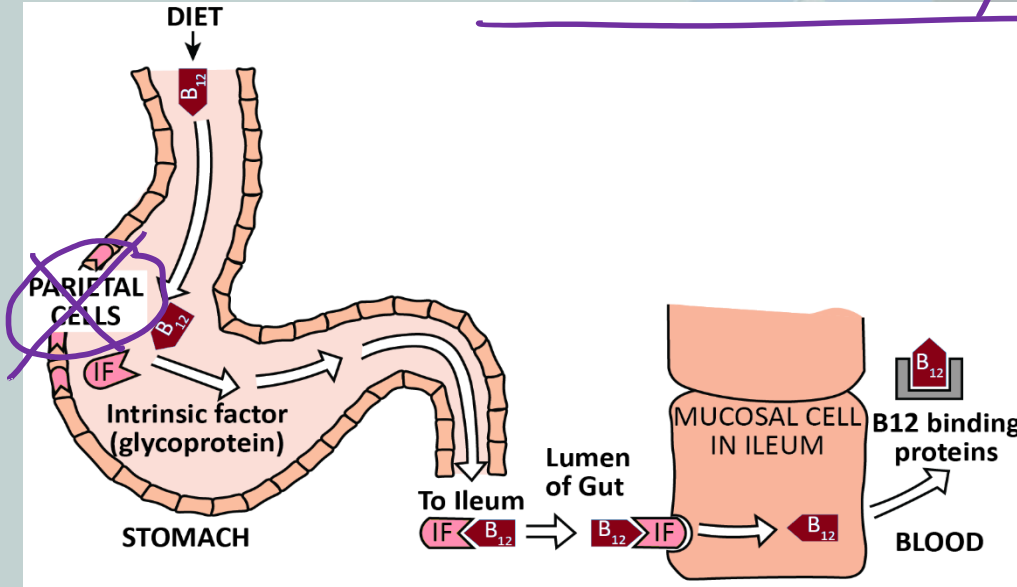
→ Homocystinuria
 → megaloblastic
anemia

Megaloblastic anemia: Folate trap hypothesis



Perinaceous anemia

Not a dietary deficiency of vit B_{12}
 Failure of vit B_{12} uptake (absorption)
 • Autoimmune disorder, gastric surgery, stomach ulcers



↓
 damage to parietal cells
 ↓
 No intrinsic factor
 ↓
 No receptor mediated
 endocytosis of B_{12} -IF



Now not recognized as Vitamin:

- Vitamin B4 (also known as adenine)
- Vitamin B8 (also known as inositol)
- Vitamin B10 (para amino benzoic acid – PABA)
- Vitamin B11 (salicylic acid)



ASCORBIC ACID (VITAMIN C)

[obtained from citrus fruits]

- Simple sugar acid
- Role as a reducing agent and antioxidant.

Neutralize ROS \rightarrow H_2O_2 , O_2^-
(Reduce)

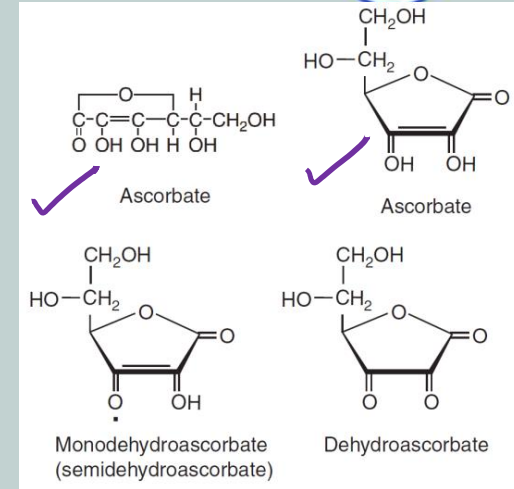
Function as co-enzyme

Dopamine β -hydroxylase is a copper-containing enzyme involved in the synthesis of the catecholamines **norepinephrine** and **epinephrine**.

Peptidylglycine hydroxylase (peptide hormones)

Proline and lysine hydroxylases

\rightarrow collagen

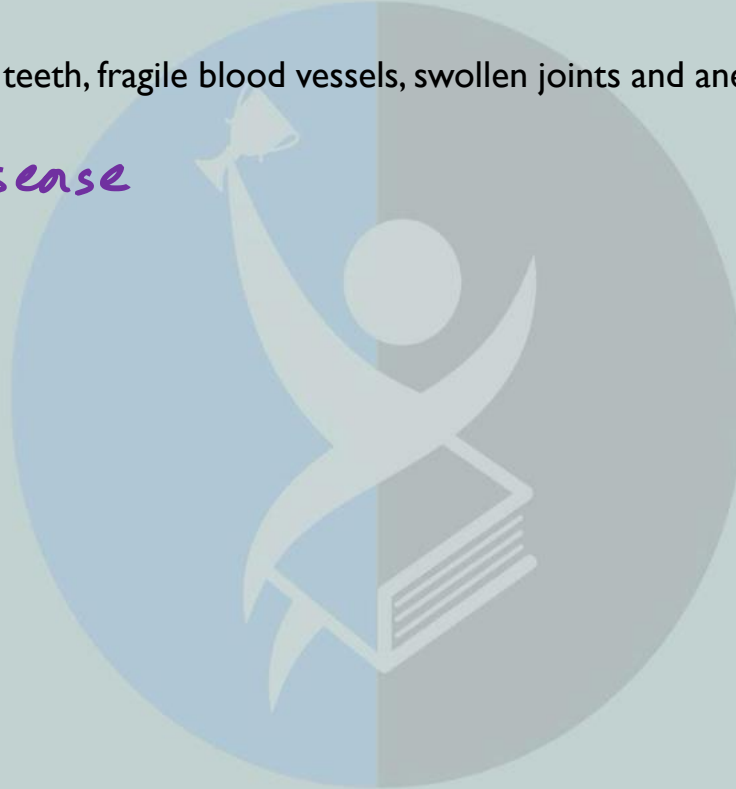




Deficiency of ascorbic acid

Scurvy: Sore, spongy gums, loose teeth, fragile blood vessels, swollen joints and anemia.

↳ *Sailor's disease*





Thank you

Learn From India's Best Educators
India's **No.1** EdTech Company for Graduates
& Post Graduates Examination.

➡ Download **IFAS** App Now



ANDROID



IOS



WINDOWS



Harshada Sharma

Earned: ₹25,500

"As is widely recognized, IFAS stands as India's leading institute for CSIR NET examination preparation. My Personal philosophy has always revolved around helping others and I've had the pleasure of introducing the IFAS Online Course to 12 of my classmates and juniors, which in turn allowed me to earn 25,500 rupees. You too can join in and refer your friends, allowing you to earn a 5% rewards based on the fees each of your referred friends Pay"



Step – 01 Invite Friends

Share your referral code or Link with your friends.

Step – 02 Earn Cashback

On Every Purchase made using your referral code, you earn 5% instant cashback in your bank account.

Step – 03 Refer More, Earn More

Keep referring as many friends as you can and keep **Earning** cash as much as you can



Friendship is Sharing, Caring, Giving & Helping Each Other...!